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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,828	01/24/2002	Carlos Plata-Salaman	ORT-1573	3409

7590 08/26/2003

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EXAMINER
MCINTOSH III, TRAVISS C

ART UNIT	PAPER NUMBER
1623	6

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	10/056,828	PLATA-SALAMAN ET AL.	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The Examiner in charge of the U.S. Patent application SN 10/056,828 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Art Unit 1623, to the attention of Traviss C. McIntosh III.

The Amendment filed May 19, 2003 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claim 13 has been amended.

Claims 23 and 24 are cancelled.

Remarks drawn to rejections of Office Action mailed December 19, 2002 include:

101 and 112 2nd paragraph rejections: which have been withdrawn due to applicant's cancellation of claims 23-24.

103(a) rejection: which has been maintained for reasons of record.

An action on the merits of claims 1-22 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

The rejection of claims 1-22 as being rejected under 35 U.S.C. 103(a) as being unpatentable over Shank et al. (WO 00/61138 A1) in view of Sachdeo et al. (Topiramate:

Clinical profile in Epilepsy, Clin. Pharmacokinet, May 1998, 34(5) pp. 335-346) and further in view of Brines et al. (WO 00/66164) is maintained for reasons of record.

Claim 1 of the instant application is drawn to a method of treating a neurological dysfunction in a subject in need thereof comprising co-therapy with a fructopyranose sulfamate and erythropoietin, wherein the amounts of the active agents are selected to produce a synergistic effect. Dependent claim 2 limits the fructopyranose sulfamate to topiramate. Dependent claim 4 limits the erythropoietin to epoetin alfa. Dependent claim 19 provides the limitations of claims 2 and 4. Dependent claims 3 and 5 limit the amounts of fructopyranose sulfamate and erythropoietin to 10-1000mg and 1-15,000 I.U./kg respectively. Dependent claims 6-18 limit the neurological dysfunction to specific, known neurological disorders. Claims 20 and 21 are drawn to compositions comprising topiramate, erythropoietin, and a carrier. Claim 22 is drawn to a method of making a composition by mixing topiramate, erythropoietin, and a carrier.

Shank et al. teach of a method for treating a variety of chronic neurodegenerative disorders comprising administering a sulfamate carbohydrate (claim 1) (a topiramate derivative). The dosage amounts in Shank et al. for the compounds of Formula I in claims 1 and 2 to be used in the method substantially overlap with applicant's asserted ranges for therapeutic concentrations. Shank et al. suggests the combination of multiple active agents to treat neurological disorders (pg 7, lines 4-8). What is not taught by Shank et al. is the coadministration of topiramate and erythropoietin.

Sachdeo et al. teaches the use of topiramate as adjunctive or combination therapy, for treating epilepsy, a known neurological dysfunction (pg. 2, lines 8-9). The dosage amounts in Sachdeo et al. for the compounds to be used in the method overlap substantially with applicant's

asserted range for therapeutic concentrations (pg. 340, lines 22-26). Sachdeo et al. do not teach to use the topiramate compound in conjunction with the specific erythropoietin compounds of the instant application.

Brines et al. teaches of compositions and methods for modulation and protection of excitable tissue, including neuronal tissue of the central and peripheral nervous system, and for the enhancement of cognitive function by administering erythropoietin, erythropoietin derivatives, and/or recombinant erythropoietin (page 9, lines 24-26). Epoetin alfa is known in the art as a recombinant form of erythropoietin. The dosage amounts of Brines et al. to be used in the method substantially overlap with applicant's asserted ranges for therapeutic concentrations (page 23, lines 28-30).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Shank, Sachdeo, and Brines and obtain a composition comprising a fructopyranose sulfamate (specifically topiramate) and erythropoietin, each of which are recognized individually for treating neurological disorders, and administer the combination composition to treat neurological disorders, because the individual active agents are taught to be effective. It requires little more than routine skill in the art to combine art recognized active agents and administer the combined composition to accomplish the same task, which is to treat neurological disorders and related symptoms and conditions, since the art discloses these agents are individually used to treat neurological disorders and since Sachdeo provides the suggestion to administer multiple agents for treating neurological dysfunction.

The thrust of applicant's arguments are drawn to the following criteria: 1) there is no motivation to combine the references, and 2) the references fail to provide a reasonable expectation of success.

1). There is no motivation to combine the references:

Applicants state (page 9, top paragraph of applicants reply) that "it appears to be the Action's position, that if a combination of therapies is claimed, and the references individually suggest the use of each agent alone, then it is obvious to combine the two agents for treatment. Applicants contend that such a position is untenable." However, the examiner notes there is case law that states it is obvious to combine individual compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. See ***In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069 (CCPA 1980).*** In the instant case, both topiramate and erythropoietin are taught to be effective against neurological/neurodegenerative diseases, therefor it would be obvious to one of skill in the art to combine the individual compositions to form a new composition which would be effective in treating neurological/neurodegenerative diseases.

2) The references fail to provide a reasonable expectation of success:

Applicants state that the combination of references does not provide a reasonable expectation of success, and in fact that Sachdeo actually teaches away from the methods of the instant invention (page 9, middle paragraph of applicant reply). Applicants then note that the author (Sachdeo) does indeed conclude that in some instances, topiramate is effective in adjunctive therapy with other AEDs. Applicants then point out various instances in which they believe Sachdeo teaches away from the instant application. For example, Sachdeo shows a total

of 46% of patients receiving 1000 mg/day of topiramate in a monotherapy regime achieved a seizure reduction of greater than 50%, whereas only 38-52% of patients receiving adjunctive therapy of 1000mg/day achieved a seizure reduction of greater than 50%. Applicants then state it is impermissible to pick and choose from a reference only what will support a given position, and exclude other parts necessary for the full appreciation of what the reference fairly suggests to one of ordinary skill in the art. The examiner agrees with this statement and notes that even in applicants own example, Sachdeo provides a reasonable expectation of success, as there were 38-52% of patients who received a greater than 50% decrease in seizures when obtaining an adjunctive therapy in relation to only 46% who underwent monotherapy. Obviousness does not require absolute predictability. This 38-52% includes 47-52%, which would provide a reasonable expectation of success to one of ordinary skill in the art reading the reference objectively. Applicant's own disclosure shows that some specific combinations are not as effective in their adjunctive form as they are in their independent forms as well as show that the combination is more effective than the individual treatments (see tables). The prior art should be read and taken into account for what it provides, and Sachdeo clearly suggests the use of topiramate as adjunctive or combination therapy, for treating known neurological dysfunctions.

Applicants then argue that the combination of erythropoietin and topiramate produces unexpected results in that the combination produces a synergistic effect and actually has a greater effect in adjunctive therapy than the effects obtained from individual therapies. However, one of ordinary skill in the art, when combining active agents known in the art to independently treat identical conditions with correlative concentrations of the active agents, would expect that the results obtained would provide some synergy of action if correlative amounts of each component

separately would indeed provide therapy for neurological conditions when combined to provide a co-administration to a patient in need thereof.

Conclusion

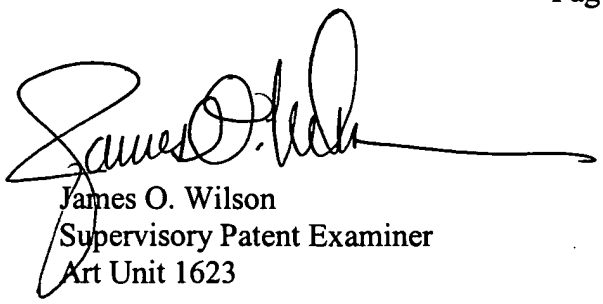
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623

Traviss C. McIntosh
August 18, 2003